acknowledged in response to the present remarks. Applicants also thank the Office for withdrawing the previous rejections of the claims under 35 U.S.C. §§ 103 and 112.

Rejection of Claims 1-11 under 35 U.S.C. § 112, First Paragraph

The Office rejects claims 1-11 as allegedly not enabled throughout their full scope. (Office Action at pages 2-3.) The Office asserts that the specification does not enable one of ordinary skill in the art to make all of the claimed heterocyclic derivatives, particularly O-heterocyclic derivatives. Applicants traverse this rejection.

The Office's position seems to be that Applicants should provide a working example to show how to make each type of heterocyclic derivative listed in claim 1. ("The specification does not give any guidance as to how each of the heterocyclic substituted derivatives was prepared." Office Action at page 2.) However, Applicants note that the enablement requirement is satisfied as long as the specification discloses at least one method for making the claimed invention that bears a correlation to the scope of the claims that is reasonable. M.P.E.P. § 2164.01(b); *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970). A patent application is not meant to be a blueprint for the claimed invention. M.P.E.P. §§ 2164.01 and 2164.08; *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991). For example, in *In re Angstadt*, 190 U.S.P.Q. 214 (C.C.P.A. 1976), the court stressed that not every species encompassed by the claims, even in the unpredictable arts, need be disclosed. Thus, a working example of a particular embodiment is not necessary if one of ordinary skill in the art can make the claimed embodiment without undue experimentation. M.P.E.P. § 2164.02. Moreover, the enablement standard leaves considerable room for experimentation, provided that it is routine, or that the application gives sufficient

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information as to the direction in which the experimentation should proceed. *See* M.P.E.P. § 2164.06.

Applicants submit that the instant specification provides more than adequate support for one of ordinary skill in the art to prepare the claimed compounds. A general procedure for preparing the compounds is provided in the specification beginning at page 34, and is also recited in claim 7. As described in paragraph 58, at pages 34-35, the claimed compounds of the formula I may be formed by linking together three smaller building block compounds of the formulas II, III, and IV. Compounds of the formulas II and III may be reacted together to form an intermediate compound reactive with a compound of formula IV. (Paragraphs 62, 63, and 64.) Alternatively, formula III and IV compounds may first be reacted together, then linked to a formula II intermediate. (*Id.*) Paragraphs 65 and 66 provide further guidance in performing these coupling reactions, by listing potential solvents and protecting groups. Further, compounds of the formulas II, III, and IV "are commercially available or can be readily prepared from commercially available compounds by or analogously to procedures described below or in the literature which is readily available to those skilled in the art." (Paragraph 61.)

By asserting that "there is insufficient enabling disclosure to support the terms heterocyclyl R," the Office appears to contend that the application does not enable all of the compounds which contain a "Het" group at position(s) R^4, R^5, or R^{10} of the claimed formula I compounds. (Applicants note that the term "heterocyclyl" R does not expressly appear in the pending claims.) As recited in claim 1, "Het is a residue of a saturated or unsaturated monocyclic or bicyclic, 3-membered to 10-membered heterocyclic ring system containing 1, 2, or 3 identical or different ring heteroatoms

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chosen from nitrogen, oxygen and sulfur." (*See also* paragraphs 22-29.) "Het" may comprise aliphatic and/or aromatic ring systems. (*Id.*) Because the "Het" groups at R^4, R^5, and/or R^{10} would be present in the formula IV precursor, the Office essentially contends that the specification does not provide guidance for making all of the formula IV compounds or for linking them to the formula III or formula II/III intermediates. However, the Office provides nothing more than conclusory statements in support of this contention.

Applicants respectfully point our that a patent application is presumptively enabled when filed. *In re Marzocchi*, 139 U.S.P.Q. 367, 369 (C.C.P.A. 1971). The Office must establish, through adequate evidence and reasoning, a *prima facie* case of non-enablement. Here, the Office has not provided any scientific rationale or evidence consistent with the substantial evidence standard of *In re Zurko*, 46 U.S.P.Q.2d 1691 (Fed. Cir. 1998), showing how the heterocyclic compounds of claims 1-12 are not enabled by the specification. Instead, the instant Office Action merely lists the factors from *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988), without any explanation as to how they apply to the present facts, and makes a conclusory statement that "one skilled in the art would have [to] speculate how derivatives were obtained or prepared." (Office Action at pages 2-3.) Therefore, Applicants submit that the Office has failed to meet its burden to establish a *prima facie* case of non-enablement.

Moreover, Applicants submit that one of ordinary skill in the art may prepare such formula IV precursors without undue experimentation. First, paragraph 61 expressly points out that formula IV compounds, as well as formula II and III compounds, "are commercially available or can be readily prepared from commercially available

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compounds," such as with procedures analogous to those described in the specification or known in the literature. Applicants submit that it does not require undue experimentation for those skilled in the art to envision formula IV intermediates that may be prepared from commercially available starting materials and known reaction protocols. Indeed, courts have long recognized that enabled claims may be described with broad language, so long as those of skill in the art can recognize the operable embodiments they comprise without undue experimentation. *See, e.g., Atlas Powder Co. v. du Pont de Nemours & Co.*, 224 U.S.P.Q. 409, 414 (Fed. Cir. 1984); *In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976); *see also* M.P.E.P. § 2164.08(b).

Second, organic chemistry textbooks known to those in the art, such as J. March, *Advanced Organic Chemistry, 4th Ed.*, referred to at paragraph 65 of the specification, provide details and literature sources for a large variety of chemical transformations that may be used to prepare formula IV intermediates. For example, one could purchase or prepare a substituted or unsubstituted nitrogen, oxygen, or sulfur-containing saturated or unsaturated heterocycle, then attach an amine substituent to it, either directly, or indirectly via attachment of a group, such as a nitro or cyano moiety, that can subsequently be transformed into an amino group. This yields an appropriate formula IV compound that will form an amide linkage with a formula III compound. The enclosed chart from S. Ege, *Organic Chemistry, 2nd Ed.*, 1989, shows a summary of standard methods of forming alkyl and aryl amines starting from a variety of other moieties. (Exhibit A.) For example, one method of aminating aromatic O, S, and N heterocycles such as thiophene, furan, and pyridine, is by reaction with nitrous oxide followed by reduction of the resulting nitro substituent to form an amine. (Exhibit B.) In

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addition, one may, for example, prepare an amino group by reductive amination, starting from a carbonyl group. (See Exhibit A at page 931, top panel of chart.) This method is well known to those skilled in the art, and allows for the preparation of many different amines containing acyclic, heterocyclic and/or carbocyclic groups. Example 49, step c, shows a reductive animation in detail. (Specification at pages 64-5.) Finally, as to forming the heterocycles themselves, substituted or unsubstituted nitrogen, oxygen or sulfur-containing heterocycles may be obtained, for example, from simpler compounds as shown in the chart at Exhibit C. If one of these simpler compounds is itself a substituent of a ring system, a more complex heterocycle may be formed. (Exhibit C.)

Applicants also submit that there is more than adequate guidance in the application for one of ordinary skill in the art to condense appropriate "Het"-containing formula IV compounds with formula III or formula II/III compounds. The working examples in the application show examples of how to prepare the amide linkage between the formula III and IV intermediates in a variety of structural contexts, for example, where R^4 and/or R^5 is a phenyl, which, in turn, may be substituted with an alkyl, amine, halogen, carbamimidoyl, or piperidine, or may be fused to another ring system. (*See, e.g.*, examples 1-3, 49, and 68.) Paragraphs 64-67 provide additional guidance as to examples of suitable solvents and protecting groups. The specification also notes that those familiar with peptide chemistry would recognize appropriate methods to form the necessary amide linkage between the formula III and IV intermediates. (Paragraph 64.)

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Thus, for all of the above reasons, the full scope of claims 1-12 is enabled. If the Office maintains that the claims are not enabled, Applicants respectfully request that the Examiner set forth adequate evidence and reasoning as required by the M.P.E.P. *See* M.P.E.P. § 2164.04. Otherwise, Applicants request the withdrawal of this rejection, the reconsideration and reexamination of this application, and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: February 25, 2003

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